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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 9095**
Hidehisa ASADA et al. :		Docket No. 2000_0259A
Serial No. 09/508,435	:	Group Art Unit 1644
Filed March 13, 2000	:	Examiner Patrick J. Nolan

IMMUNOASSAY FOR BNP

REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is responsive to the Official Action dated October 21, 2003.

Reconsideration is respectfully requested in view of the following remarks.

The Examiner has maintained the rejection under 35 USC 103 as being unpatentable over Hunt et al. in view of Harlow et al.

Initially, the Examiner is kindly reminded that PreProBNP is subjected to processing in living bodies to produce gamma-BNP (also known as Pro-BNP), which is in turn subjected to processing to produce alpha-BNP (also known as BNP-32).

The invention of claim 23

The invention of claim 23 is divided into the following characteristic elements:

i) the invention is directed to a sandwich immunoassay;

ii) the sandwich immunoassay is specific for detecting gamma-BNP derivatives;

iii) the gamma-BNP derivatives have both a carboxy terminus portion including alpha-BNP, and an amino terminus portion not including alpha-BNP;

iv) the sandwich immunoassay comprises use of a first antibody, and use of a second antibody,

v) the first antibody specifically reacts with the carboxy terminus portion of the gamma-BNP derivatives, and

vi) the second antibody specifically reacts with the amino terminus portion of the gamma-BNP derivatives, and does not react with the carboxy terminus portion of the gamma-BNP derivatives.

The invention of Hunt et al.

As the Examiner recognizes, Hunt et al. do not describe any sandwich immunoassay. Hunt et al. describes an immunoassay for alpha-BNP, and an immunoassay for an N-terminal fragment of gamma-BNP. In other words, Hunt et al. describe the two separate types of immunoassay. Here, it should be noted that the N-terminal fragment of gamma-BNP to be assayed in the latter immunoassay of Hunt et al. is dissociated from gamma-BNP, and does not comprise structurally the alpha-BNP moiety. This is understood from the description at lines 6-10 on page 1176 in Hunt et al. *"We hypothesized that if alpha-BNP is a direct cleavage product from gamma-BNP, then the N-terminal gamma-BNP fragment is likely to be produced along with alpha-BNP"*. Thus, Hunt et al. assayed for the N-terminal fragment by an immunoassay using one antibody directed to the fragment, so as to finally determine alpha-BNP.

Comparison between the present invention and the invention of Hunt et al.

Immunoassay of Hunt et al., wherein the antibody directed to the N-terminal fragment of gamma-BNP is used, results in the detection of all products having the N-terminal fragment, which include some products that do not comprise structurally the alpha-BNP moiety.

In contrast, the claimed invention detects only the gamma-BNP derivatives, which have not only the amino terminal fragment but also alpha-BNP at the carboxy terminus, and which exclude mere N-terminal fragments that do not comprise structurally the alpha-BNP moiety.

In order to assay for the gamma-BNP derivatives, the present invention is directed to a sandwich immunoassay as defined in item i) above, and comprises use of both the first antibody which specifically reacts with the carboxy terminus portion of the gamma-BNP derivatives, as defined in item v) above, and the second antibody which specifically reacts with the amino

terminus portion of the gamma-BNP derivatives, and does not react with the carboxy terminus portion of the gamma-BNP derivatives, as defined in item vi) above.

Gamma-BNP derivatives have been selected as the object to be measured according to the present invention based on the finding by the present inventors that BNP exists in blood in the form of gamma-BNP or its degradation product which at least comprises structurally the alpha-BNP moiety (gamma-BNP derivatives). See the specification from line 26 on page 3 to line 3 on page 4.

Hunt et al. neither teach nor suggest that the gamma-BNP derivatives play an important role in cardiac diseases involving BNP. Therefore, there is no motivation in Hunt et al. to assay for the gamma-BNP derivatives, nor to construct a sandwich immunoassay according to this invention. In Hunt et al., it is not necessary to use a sandwich immunoassay to assay for N-terminal fragments that do not comprise structurally the alpha-BNP moiety.

In the Office Action, the Examiner has stated that the claimed invention differs from Hunt et al. by the recitation of using a sandwich assay rather than an RIA, but Harlow et al. teach sandwich assays are one of the most useful of the immunoassays, thus concluding that the claimed invention should be obvious.

However, the claimed invention differs from Hunt et al. not only by such recitation, but also by the object to be assayed as shown above. Accordingly, the Examiner's reasoning is respectfully submitted to be untenable.

According to the present invention, only gamma-BNP derivatives are assayed by sandwich immunoassay, and therefore an accurate method of diagnosing cardiac diseases involving BNP can be accomplished. Such results of the present invention should be unexpected, which is neither described nor suggested in Hunt et al.

Obviousness cannot be predicated on picking and choosing selected teachings in the prior art where there is no motivation to do so. The cited references in this case fail to motivate one skilled in the art to arrive at the claimed invention.

In view of the foregoing, favorable reconsideration and allowance is solicited.

Respectfully submitted,

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